"Nitroglycerin equivalent" is a dosage of a chosen vasodilator which dilates to the same extent as a dosage of nitroglycerin within the range stated. The parenthetical expression was merely a trademark for the generic term. The trademark has been removed without prejudice to the generic term.

> *With respect to claims 36 and 37 the claims scope is wholly unclear. This case originally contained only claims 1 - 20, all cancelled per instructions in the Preliminary Amendment filed*
> *[Page2]*
> *The Substitute Specification filed 07-02-01 has been entered to the record April 23, 2001 to cancel all prior claims. Therefore there is no claim 21 and no claim construable as being the parent claim to these claims for purposes of understanding their method scope*

References to Claim 21 have been replaced with references to Claim 32.

> *With respect to claim 38, the preamble pertains to a 'titration system' whereas the body of the claim recites only method steps non-limiting on the titration system hence the scope is wholly unclear.*
> *[Page 3]*

The method words have been deleted and Claim 38 now reads as an apparatus claim.

> *Claim Rejections - 35 USC §103*
> *3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:*
> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*
> *4. Claims 32 - 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Panoz (US4592753) in view of Stanley et al (US4885173). The former teaches the use of a patch (col. 1 lines 33 - 68) of 2% nitroglycerin or clonidine transdermal delivery system for administration*
> *of these vasodilatory agents (col. 4 lines 7-13) including treatment of systemic diseases such as*
> *hypertension. It would have been obvious to provide usage/dosage instructions with a potent prescription drug, and for example user instructions are provided, see col. 2 lines 22 - 24 and 5*
> *lines 14 - l 6 .It would have been obvious in view of Stanley et at cols.5 - 6 and col. 8 lines 29 - 37 to titrate a vasodilator dosage in view of the patent's statements and side-effects stated.*
> *[Page 2]*

Panoz (US4592753) does teach the use of a patch (col.1 lines 33 - 68) of 2% nitroglycerin or clonidine transdermal delivery system for administration of these vasodilatory agents (col. 4 lines 7-13) including treatment of *angina* with nitroglycerin (col. 4, lines 7-9) and hypertension with *clondine* col. 4 line 11).

Panoz does not mention dosage, but clearly intends to provide the conventional nitroglycerin dosage for angina, because Panoz is directed to an improved patch, not to improved treatment of a particular disease. Panoz is not directed "for treatment of diseases involving vasospasm" as recited in the present claims. Thus Panoz teaches nothing regarding treatment of the

diseases recited in the present claims, nor the reduced dosages discovered to be effective for such diseases, much less the concept of measuring blood flow to test for vasospasm, still much less the device for applying reduced dosage in response to such blood flow tests over time. In short, Panoz is not trying to solve the problem solved by the invention.

Adding Stanley does not cure the defects of Panoz. Stanley et al (US4885173) at cols.5-6 and col. 8 lines 29-37 merely teaches one to let a patient lick a medicated lollipop to administer a vasodilator dosage in view of the *patent's statements* and side-effects stated. If patents subjectively knew when they suffered vasospasms, there would be no need for the objective flow testing which is a fundamental feature of the invention, recited in the claims. Applicant has discovered that an objective test (not subjective statements) must be used to titrate dosage to achieve the valuable cures described in the Examples.
A person who read Panoz and who somehow choose to also read Stanley would still not learn how to achieve the valuable results shown in the many Examples of the Application, because the combination of testing apparatus and controlled dosage over time is not taught by either reference, alone or combined.

The Substitute Specification filed 07-02-01 has been entered to the record.
The Examiner is thanked for entering the substitute specification.

Renumbering of claims in consecutive order per Rule 126 has been held in abeyance pending understanding of status of claims 21 -31 and antecedent reference made to claim 21 in the current claims.
The reference to "Claim 21" has been deleted.

1. Any inquiry concerning this communication should be directed to Examiner Francis J. Jaworski at telephone number 703-308-3061
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Conclusion

Panoz teaches nothing regarding titration and Stanley teaches nothing regarding curing strokes, and the combination of these references would not make the present invention obvious. See, for example, Equipment Co.v. United States, 702 F.2d 1005, 217 U.S.P.Q. 193, (Fed. Cir. 1983):

> The question of nonobviousness is a simple one to ask, but difficult to answer . . . The difficulty which attaches to all honest attempts to answer this question can be attributed to the strong temptation to rely on hindsight while undertaking this evaluation. It is wrong to use the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the

result of the claims in suit. Monday morning quarterbacking is quite improper when resolving the question of nonobviousness.

No estoppel has been created by these amendments. See Mannesmann Demag Corp. v. Engineered Metal Products Co., Inc., 230 U.S.P.Q. 45 (Fed. Cir. 1986) (where a patentee's amendments were not required in response to an examiner's rejection, or critical to the allowance of the claims, no estoppel has been found) citing, Great Northern Corp. v. Davis Core & Pad Co., 782 F.2d 159, 28 U.S.P.Q. 356 (Fed. Cir. 1986) and Datascope Corp. v. SMEC, Inc., 776 F.2d 320, 227 U.S.P.Q. 838 (Fed. Cir. 1985). See also, Insta-Foam Products Inc. v. Universal Foam Systems, Inc, 15 U.S.P.Q.2d 1295 (Fed. Cir. 1990).

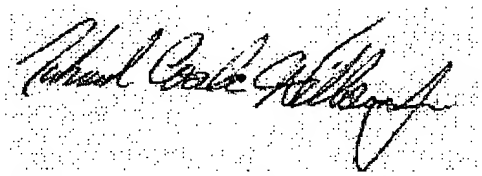
A Notice of Allowance is earnestly solicited.

Any (small entity) charges required for the prosecution of this application should henceforth be charged to USPTO Deposit Account 20-0336 of Technology Licensing Co. LLC.

Please note the address and telecontact numbers and direct all future correspondence to that address.

Please advise if anything further is required at this time.

Respectfully submitted,



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Encl: Clean set of claims

Clean Set of Claims

32. Vasodilator delivery systems specially adapted to deliver about about 0.02 to 20 milligrams per day dosage of vasodilators and marked with the appropriate DRG and/or ICD disease codes and/or instructions for titrating or tapering their use, to facilitate their proper application for treatment of diseases involving vasospasm.

33. A delivery system according to Claim 32 adapted for transdermal delivery.

34. A delivery system according to Claim 38 adapted for the adjusting of the dosage device over time within the range of about 0.02 to 20 milligrams per day (Nitroglycerin equivalent) of vasodilator.

35. A delivery system according to Claim 32 adapted for delivery of about 0.02 to 20 milligrams per day (Nitroglycerin equivalent) of a vasodilator selected from the group comprising Nitroglycerin in pill, patch, ointment, cream, inhaler, spray and other forms, Nitroglycerin equivalents and substitutes, comprising p.o. clonidine, isradipine, hydrazine, nifedipine, and/or other medicines selected from the empirical group of medications which have the common characteristic of causing smooth muscle relaxation and/or which systemically reduce pulmonary capillary wedge pressure, and combinations of the foregoing.

36. A system according to Claim 32 wherein the disease is selected from the group consisting of fibromyalgia, gastric disorders and other systemic

disorders, psychosis, other psychiatric disease, attention deficit disorder and systemic disorders, comprising vasospasm as a component.

37. A system according to Claim 32 wherein the disease is selected from the group consisting of systemic disorders comprising vasospasm as a component.

38. A titration system for diagnosing and treating a disease caused at least partially by insufficient cerebral perfusion, comprising in combination: a flow measuring device to test for vasospasm, a dosage device which administers a vasospasm-reducing dosage of a medicine selected from the empirical group of medications which have the common characteristic of causing smooth muscle relaxation and/or which reduce pulmonary capillary wedge pressure, and said dosage device being adjustable over time to titrate said dosage in response to said testing to minimize occurrence and severity of said vasospasm.

39. A system according to Claim 38 wherein the flow measuring device comprises transcranial doppler measuring means.

40. A system according to Claim 38 wherein the dosage device comprises means for delivering a vasodilator selected from the group comprising Nitroglycerin in pill, patch, ointment, cream, inhaler, spray and other forms, Nitroglycerin equivalents and substitutes, comprising p.o. clonidine, isradipine), hydrazine, nifedipine, and/or other medicines selected from the empirical group of medications which have the common characteristic of causing smooth muscle relaxation and/or which systemically reduce pulmonary capillary wedge pressure, and combinations of the foregoing.

41. A system according to Claim 38 wherein the flow measuring device comprises transcranial doppler measuring means and inhaler, spray and other forms, Nitroglycerin equivalents and substitutes, comprising p.o. clonidine, isradipine, hydrazine, nifedipine, and/or other medicines selected from the empirical group of medications which have the common characteristic of causing smooth muscle relaxation and/or which systemically reduce pulmonary capillary wedge pressure, and combinations of the foregoing.

42. A system according to Claim 41 wherein the delivery device comprises means for delivering a vasodilator selected from the group comprising Nitroglycerin in pill, patch, ointment or cream form.

43. A system according to Claim 38 wherein the delivery systen is adapted for transdermal delivery.

44. A system according to Claim 38 wherein the delivery system is adapted for the adjusting of the dosage device over time within the range of about 0.02 to 20 milligrams per day (Nitroglycerin equivalent) of vasodilator.

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